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PROTECTION, REPAIR AND REGENERATION OF ACHYBREAKY HEART

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Pasquale Pagliaro and Claudia Penna

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality worldwide. Therefore, there is an urgent need to find appropriate strategies to afford cardioprotection. Cardiovascular health may be preserved and CVD can be fought with interventions aimed at protection, repair and regeneration of the heart. Despite great advances in treatment of patients with atherosclerosis and coronary heart disease, heart failure (HF) is still a huge problem. HF is a complex multifactorial syndrome, which may be caused by several clinical conditions, including coronary ischemic disease. It is often associated with one or more comorbidities and is characterized by several overlapping pathophysiological features. These include cardiac systolic and diastolic contractility abnormalities, occurrence of arrhythmias and organ hypoperfusion, as well as endothelial and vascular dysfunction, autonomic impairment, and neurohormonal imbalances. HF displays the greatest negative impact on the efficiency of a subject leading to the disruption of daily functioning and increasing dependence on caregivers. In particular, in our aging population, HF is a serious problem for the society, affecting the quality of life of millions of people. In view of the intolerable burden required to the society, there is an urgent need to develop new treatments to reduce the toll from coronary heart disease and HF and to improve the life quality of individuals. To achieve this goal, new and effective therapeutic approaches are required, but to achieve the latter multidisciplinary approaches are required that aim at defining the signaling mechanisms and molecular interactions that address myocardial tissue towards a cardio-vascular protective phenotype [1]. In this special issue "Protection, Repair and Regeneration of Aching Heart", we highlight the known mechanisms leading to heart disease, discuss current approaches and future therapeutic strategies for targeting a damaged heart. The role of epigenetic, genomic, proteomic, and metabolomic systems biology approaches to uncover novel strategies for targeting mechanisms of myocardial damage are addressed in the context of several cardiovascular disease and in particular in the context of ischemia/reperfusion injury and atherosclerosis. Together, the review articles in this issue highlight the critical need for advancements in developing therapeutics strategies targeted at the cardiovascular system that will be effectively translated to the clinic to significantly impact CVD treatment. In particular, in their review, Urbanek et al. [2] discuss the role of resident and extracardiac progenitors in the pathogenesis of cardiomyopathies of different etiology for both a better understanding of cardiac homeostasis and to pave the way for new therapeutic approaches. The authors propose new strategies for the exploitation of the potential for self-renewal myocardial and systemic cardiogenic cells. Madonna et al. [3] discuss the genes and signaling pathways that play a crucial role in the aging of stem cells, reporting *ex vivo* approaches that consider genetic modification as a tool to rejuvenate stem cells. They also discuss innovative approaches to improve the cellular retention of interest for the cardiovascular system. Moreover, Matteucci et al. [4] discuss how the cardiovascular microenvironment exposed to various stressors can trigger epigenetic changes that affect the function, proliferation, survival, and senescence of all cardiac cells. Moccia et al. [5], analyze how intracellular Ca^{2+} signal can be targeted to redirect stem cell toward lineages able to restore cardiac vascularization and contractility. In their review, Varga et al. [6], propose a comprehensive analysis of gene expression fingerprint in normal, protected, and in comorbidity conditions and propose that this analysis may lead to identification of novel molecular targets for cardioprotection. Several, endogenous factors, signaling pathways and possible targets involved in cardioprotection (preconditioning, perconditioning and postconditioning) are discussed by Penna et al. [7], whereas Weber et al. [8] discuss the cardioprotective signaling pathway and targets of the non-anesthetic noble gas helium. From these articles, the fundamental role played by the nitroso-redox balance in determining CVD and

cardioprotection is evident. In their review, Tocchetti et al. [9], focus on the crucial role of nitroso-redox balance in cardiac function. Given the central role of mitochondria in cardioprotection, the processes of mitochondrial fusion and fission are attracting the attention of many researchers. In this issue, the role of mitochondrial fusion protein optic atrophy protein 1 in cardiovascular health and disease is analyzed by Burke et al. [10]. These authors also explore the role of this protein as a potential therapeutic target for treating CVD. Deniset and Pierce [11] focus their attention on heat shock proteins in CVD and, in particular, in atherosclerotic vascular disease, and discuss the therapeutic potential to target these proteins to affect the natural progression of CVD. The emerging role of Nefastin-1 in affecting several cardiac functions in health and disease is discussed by Imbrogno et al. [12]. Finally, the role of hyperpolarization-activated cyclic nucleotide-gated channels in the progression of cardiac diseases, rhythm disturbances and their targeting by novel drugs to treat several conditions is discussed by Sartiani et al. [13]. Altogether, these reviews can open the way for studies aimed at identifying new selective compounds with greater selectivity as potential candidates for drug development. We hope that studies stimulated by this special issue, by exploring more efficient and protective signaling pathways and cell therapies for the improvement of heart function, will expand the current list of treatments and options to prevent or revert cardiomyopathies. Editorial Current Drug Targets, 2015, Vol. 16, No. 8 779

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REFERENCES

- [1] Lazzarini V, Mentz RJ, Fiuzat M, et al. Heart failure in elderly patients: distinctive features and unresolved issues. *Eur J Heart Fail* 2013; 15: 717-23.
- [2] Urbanek K, Frati C, Graiani G, et al. Cardioprotection by Targeting the Pool of Resident and Extracardiac Progenitors. *Curr Drug Targets* 2015; 16(8):884-94.
- [3] Madonna R, Engel FB, Davidson SM, et al. Stem cell aging and age-related cardiovascular disease: Perspectives of treatment by ex-vivo stem cellrejuvenation. *Curr Drug Targets* 2015; 16(8): 780-5.
- [4] Matteucci M, Papini G, Ciofini E, et al. Epigenetic Regulation of Myocardial Homeostasis, Self-Regeneration and Senescence. *Curr Drug Targets* 2015; 16(8): 827-42.
- [5] Moccia F, Ruffinatti FA, Zuccolo E. Intracellular Ca²⁺ Signals to Reconstruct a Broken Heart: Still a Theoretical Approach? *Curr Drug Targets* 2015;16(8): 793-815.
- [6] Varga ZV, Giricz Z, Bencsik P, et al. Functional genomics of cardioprotection by ischemic conditioning and the influence of comorbid conditions:implications in target identification. *Curr Drug Targets* 2015; 16(8): 904-911.
- [7] Penna C, Granata R, Tocchetti CG, et al. Endogenous Cardioprotective Agents: Role in Pre and Postconditioning. *Curr Drug Targets* 2015; 16(8): 843-67.
- [8] Weber NC, Smit KF, Hollmann MW, et al. Targets Involved in Cardioprotection by the Non-Anaesthetic Noble Gas Helium. *Curr Drug Targets* 2015;16(8): 786-792.
- [9] Tocchetti CG, Molinaro M, Angelone T, et al. Nitroso-Redox Balance and Modulation of Basal Myocardial Function: an Update from the ItalianSociety of Cardiovascular Research (SIRC). *Curr Drug Targets* 2015; 16(8): 895-903.
- [10] Burke N, Hall AR, Hausenloy DJ. OPA1 in Cardiovascular Health and Disease. *Curr Drug Targets* 2015; 16(8): 912-20.
- [11] Deniset JF, Pierce GN. Heat shock proteins: Mediators of atherosclerotic development. *Curr Drug Targets* 2015; 16(8): 816-26.

- [12] Imbrogno S, Angelone T, Cerra MC. Nesfatin-1 and the cardiovascular system: central and peripheral actions and cardioprotection. *Curr Drug Targets* 2015; 16(8): 877-883.
- [13] Sartiani L, Romanelli MN, Mugelli A, et al. Updates on HCN Channels in the Heart: Function, Dysfunction and Pharmacology. *Curr Drug Targets* 2015; 16(8): 868-76.

Pasquale Pagliaro, M.D., Ph.D. and Claudia Penna, Ph.D.

(Editors)

Department of Clinical and Biological Sciences,

University of Torino

AOU San Luigi Gonzaga

Regione Gonzole, 10, 10043 Orbassano,

Italy

Tel: +39 011 6705450-5430

E-mails: pasquale.pagliaro@unito.it, claudia.penna@unito.it